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Circadian Variations of Blood Pressure in Acute Stroke Patients Treated at Adam Malik Hospital of Medan

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Several studies have shown that absence of blood pressure variation during sleep is associated with target organ damage including organ damaged sustained as a result of cerebrovascular accidents. In the management of stroke associated with hypertension, antihypertensive medications should be carefully administered because they may cause extensive damage to the brain. Twenty-four hour blood pressure monitoring is important. To investigate circadian variations in the blood pressure of stroke patients, a cross-sectional study was conducted. A sample of 30 patients who presented within 1-7 days of symptom onset and were aged 40 years or more was selected. The study participants' blood pressures were measured by ambulatory monitoring. Personal and medical information were collected. Data analysis was performed using SPSS version 20.0. The Pearson Chi square test was used to analyze differences in the circadian patterns of blood pressure according to age, sex, type of stroke and both the onset and frequency of symptoms. An independent t-test was used to analyze differences in mean blood pressure. The results revealed that hypertension is major risk factor for stroke patients with a non-fluctuating pattern of blood pressure. Nondippers were more common than dippers. Nondippers were comprised 80, 90 and 83.3% of systolic, diastolic and mean arterial pressure groups. There were no significant differences in circadian patterns and mean blood pressure by age, sex, onset and frequency of symptoms and the type of stroke. These results indicate that the circadian rhythm of blood pressure is important in the management of hypertension.

Key words: Circadian, variation, acute stroke

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INTRODUCTION

Hypertension is the most important risk factor for stroke (Caplan, 2000; Jain et al., 2000) and is also a prognostic indicator in patients who have suffered a stroke (Jain et al., 2000). Hypertension plays a role in arterial occlusion, embolic stroke and the rupture of causes cerebral aneurysms, which intracerebral hemorrhage (Sacco and Albala, 2001). In the majority of patients with hypertension, the most common blood pressure pattern, also known as a nondipper pattern, is characterized by the absence of a night-time blood pressure decrease (Kario et al., 1996). Several studies have shown that this blood pressure pattern is more closely associated with damage to both cardiovascular and cerebrovascular organs (Caplan, 2000; Jain et al., 2000).

Target organ damage in hypertension is closely related to blood pressure measurements taken over 24 h or ambulatory blood pressure (Mancia and Parati, 2000; Verdecchia et al., 1994). Yamamoto et al. (1998) studied 105 stroke patients who suffered lacunar infarcts and found that high blood pressure, particularly blood pressure elevated at night, may lead to an increased number of ischemic lesions and lacunar infarcts. Kario et al. (2003) studied 519 older hypertensive patients and found that a morning surge in blood pressure was associated with stroke events, independent of 24 h blood pressure monitoring. Moreover, Ohkubo et al. (2000) found that ambulatory blood pressure was a strong predictor of stroke risk. Therefore, blood pressure control over a 24 h period in patients with hypertension is necessary for both the management of hypertension (White, 2007) and the prevention of stroke and stroke recurrence (Kalim, 2009).

Circadian variations in blood pressure are recognized as prognostic markers in hypertensive patients. This rhythm is influenced by several factors, including hemodynamic and neurohumoral factors, as well as other factors (Ajayi et al., 2013). Circadian rhythm is characterized by a reduction in several biological parameters during sleep and a rise in these parameters upon waking. Circadian rhythm may be observed in both normotensive and hypertensive patients but it does not always manifest (Larochelle, 2002). Several studies have described circadian patterns associated with stroke (Lago et al., 1998; Elliott, 1998; Yung et al., 2007; Anderson et al., 2004). In the management of hypertension, achieving blood pressure control is important because it may minimize or block the effects imposed by an abnormal circadian pattern (White, 2007).

Antihypertensive medications have preventive effects on the progression of hypertensive arterial lesions

but they are also likely to cause decreased blood flow to an area supplied by stenotic atherosclerotic arteries and increase the risk of stroke recurrence (Yamamoto et al., 1998; Nakamura et al., 1995; Grassi et al., 1998). Nakamura et al. (1995) studied 76 patients who suffered an ischemic stroke (43 receiving anti-hypertensives and 33 not receiving antihypertensives) and found that 6 patients taking anti-hypertensive medication suffered recurrent strokes (1 with a nondipper pattern and 5 with a dipper pattern), whereas 10 patients suffered recurrent strokes in the group not taking antihypertensive (8 with a non dipper pattern and 2 with a dipper pattern). These results indicate that hypertensive patients with nocturnal blood pressure decreases treated with anti-hypertensives are at increased risk for ischemic brain lesions (Nakamura et al., 1995). In a study of elderly patients with hypertension, Watanabe et al. (1996) found that excessive decreases in nocturnal blood pressure are associated with the occurrence of silent ischemic cerebrovascular lesions, particularly in elderly women. These findings showed that the management of hypertension must be handled with care where nocturnal blood pressure is concerned.

In the management of acute stroke patients with hypertension, the reduction of arterial blood pressure must be handled carefully. Excessive blood pressure cause ischemic brain lesions lowering may (Yamamoto et al., 1998). Moreover, circadian rhythm is important in this process. Therefore, 24 h blood pressure monitoring is necessary to determine the relationship between circadian rhythm and blood pressure to properly dose antihypertensive medications and prevent stroke and recurrent stroke. Therefore, a study to analyze circadian variations in blood pressure in patients who suffered acute stroke and were treated at Adam Malik Hospital of Medan was undertaken to help clinicians make appropriate decisions regarding the use antihypertensive in managing stroke associated with hypertension.

MATERIALS AND METHODS

Study protocol and recruitment: This was a cross-sectional study involving patients who were diagnosed with stroke and treated in the Neurological Department of Haji Adam Malik Hospital (Medan, North Sumatera), from October to December 2004. Subjects who had specific symptoms underwent a full history, physical examination and neuroimaging (head CT) to confirm the diagnosis of stroke. Patients were consecutively enrolled in this study according to following criteria; 40 years of age or older and willing to participate in this study and admitted to the hospital within 1-7 days of symptom onset. Patients with the following conditions were excluded; age less than

40 years old, subarachnoid hemorrhage, intracerebral hemorrhage greater than 60 mL, symptoms for more than 7 days prior to hospital admission, atrial fibrillation or cardiac failure, Parkinson disease and unwillingness to participate in this study. Patients who met the inclusion criteria underwent 24 h blood pressure monitoring. The medical history and personal information of each patient were collected and recorded via questionnaire. Study population were divided according to the median of age. Kario et al. (1996) found that in elderly patients with hypertension, the blood pressure pattern is characterized by the absence of a night-time blood pressure decrease. Meanwhile, Watanabe et al. (1996) found excessive decreases in nocturnal blood pressure in the management of hypertension are associated with the occurrence of silent ischemic cerebrovascular lesions.

Stroke diagnoses: Stroke was diagnosed based on clinical features and neuroradiologic images (Caplan, 2000). Stroke patients were classified as having either hemorrhagic or ischemic stroke using the World Health Organization criteria (WHO, 1978). Stroke onset time was defined as the earliest time at which each patient noticed neurological deficits or symptoms. For patients who first noticed their symptoms upon waking, it was presumed that their strokes had occurred during sleep. Stroke onset was divided into two groups depending on whether the event occurred during the day or at night. Day was 6 a.m. to 10 p.m., whereas night was 10 p.m. to 6 a.m. (Lago et al., 1998).

Dippers and nondippers blood pressure determination:

Subjects who met the inclusion criteria underwent 24 h blood pressure monitoring to determine whether their blood pressure pattern matched those of dippers or nondippers. Nondippers were defined as patients with a <10% decrease in average evening blood pressure compared with the average daytime blood pressure, whereas dippers were defined as having a decrease in night-time blood pressure greater than 10% compared with the average day time blood pressure (Kario *et al.*, 2000). The mean daytime (6 a.m. to 10 p.m.) and night-time blood pressures (10 p.m. to 6 a.m.) were labeled as active and passive blood pressures, respectively (Von Kanel *et al.*, 2004). The average blood pressure over 24 h (day time and night time) was the total blood pressure (Jain *et al.*, 2000).

Statistical analysis: The SPSS package program, version 20.0, was used for statistical analysis. Descriptive analysis was used to describe the characteristic of acute stroke

patients, characteristic of the disease and changes in blood pressure in acute stroke patients. An independent t-test was used to analyze differences in mean blood pressure by age, sex, type of stroke and onset and frequency of symptoms. The Pearson Chi square test was used to analyze differences in the circadian patterns of blood pressure dippers and nondippers according to age, sex, type of stroke and onset and frequency of symptoms. A p-value less than 0.05 was considered statistically significant.

RESULTS

The mean age of the study population was 58.6±10.1 years (range 41-82 years). Most (60%) patients were men and ten patients (33.3%) were members of the Batak Karo ethnic group (Table 1).

The majority of patients (73.3%) were diagnosed with ischemic stroke and the remaining patients (26.7%) were diagnosed with hemorrhagic stroke. Most of those patients suffered their first stroke (73.3%) and the onset of their symptoms occurred mostly during the day (66.7%). Risk factors included hypertension (86.7%), family history of stroke (13.3%), diabetes (13.3%) and hypercholesterolemia (10.0%) (Table 2).

The circadian pattern of blood pressure in acute stroke is depicted in Fig. 1. The relative numbers of nondippers and dippers were depicted in Fig. 2. There were more nondippers than dippers. The mean total systolic blood pressure was 153.7±28.9 mm Hg; active systolic blood pressure was 155.6±27.7 mm Hg and passive systolic blood pressure was 150.2±31.9 mm Hg. The mean total diastolic blood pressure was

Table 1: Characteristics of acute stroke patients

Characteristic	No.	Percentage
Age (years)	58.6	10.1° 57°
41-47	4.0	13.4
48-54	7.0	23.3
55-61	7.0	23.3
62-68	6.0	20.0
60-75	5.0	16.7
76-82	1.0	3.3
Sex		
Men	18.0	60.0
Women	12.0	40.0
Race		
Batak toba	7.0	23.4
Batak simalungun	1.0	3.3
Batak mandailing	3.0	10.0
Batak karo	10.0	33.3
Batak nias	1.0	3.3
Melayu	2.0	6.7
Aceh	3.0	10.0
Jawa	2.0	6.7
Tamil	1.0	3.3

aMean (SD), bMedian

	eristics	

Characteristics of disease	No.	Percentage
Type of stroke		
Hemorrhagic stroke	8	26.7
Ischemic stroke	22	73.3
Family history of stroke		
Yes	4	13.3
No	26	86.7
History of hypertension		
Yes	26	86.7
No	4	13.3
Taking an antihypertensive		
Yes	20	66.7
No	10	33.3
History of diabetes		
Yes	4	13.3
No	26	86.7
History of hypercholesterolemia		
Yes	3	10.0
No	27	90.0
Frequency of stroke		
First	22	73.3
Recurrent	8	26.7
Onset of stroke		
During the day	20	66.7
At night	10	33.3

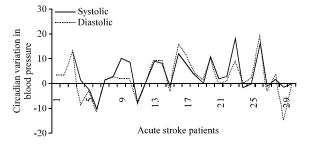


Fig. 1: Circadian patterns of blood pressure in acute stroke

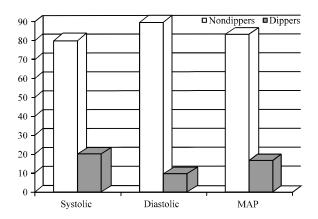


Fig. 2: Proportions of each circadian pattern for blood pressure measurements in acute stroke

87.9±18.1 mm Hg; active diastolic blood pressure was 88.8±17.8 mm Hg and passive diastolic blood pressure was 86.4±18.8 mm Hg (Table 3).

The nondipper blood pressure pattern was the most common pattern observed in the setting of acute stroke

Table 3: Changes in blood pressure in acute stroke patients

	Minimum	Maximum	Mean (SD)
Blood pressure		(mm Hg)	
Total systolic	103.6	203.6	153.7 (28.9)
Active systolic	105.3	203.8	155.6 (27.7)
Passive systolic	100.6	201.4	150.2 (31.9)
Total diastolic	55.8	117.9	87.9 (18.1)
Active diastolic	59.7	116.4	88.8 (17.8)
Passive diastolic	48.4	119.8	86.4 (18.8)

Table 4: Circadian patterns of blood pressure by age

	Age (y	ears)			
	≤57		>57		
Blood pressure	No.	%	No.	%	p-value
Systolic blood pressure					
Dippers	3	10.0	3	10.0	1.000
Nondippers	13	43.3	11	36.7	
Diastolic blood pressure					
Dippers	2	6.7	1	3.3	1.000
Nondippers	14	46.7	10	33.3	
Mean arterial pressure					
Dippers	3	10.0	2	6.7	1.000
Nondippers	13	43.3	12	40.0	

Table 5: Mean blood pressures by age

	Age (yea	ars)			
	≤ 5 7		>57		
Blood pressure	No.	%	No.	%	p-value
Total systolic	150.3	28.5	157.5	29.9	0.505
Active systolic	152.9	26.9	159.0	29.2	0.540
Passive systolic	145.9	31.2	155.6	33.1	0.428
Total diastolic	91.5	19.5	83.9	16.0	0.255
Active diastolic	93.0	18.3	84.1	16.6	0.172
Passive diastolic	88.8	21.4	83.4	15.3	0.449

based on systolic, diastolic and mean arterial blood pressures obtained in this study. The blood pressures of both groups were not significantly different based on age, sex, type of stroke and onset and frequency of symptoms. Nondippers were more commonly found in the group of patients aged 57 years or younger based on systolic, diastolic and mean arterial pressures compared with the patients who were older than 57 years of age. No significant difference existed in the circadian patterns of either dippers or nondippers between the age groups in question (Table 4). The mean systolic blood pressures were higher in the older age group, whereas the mean diastolic blood pressures were higher in the younger age group, although mean systolic and diastolic blood pressures were not significantly different between the groups (Table 5).

There were more male nondippers than female nondippers based on systolic, diastolic and mean arterial pressures. The mean systolic and diastolic blood pressures were higher in males than in females. However, there were no significant differences in either circadian

Table 6: Circadian patterns of blood pressure by sex

	Male		Femal	e	
Blood pressure	No.	%	No.	%	p-value
Systolic blood pressure					
Dippers	5	16.7	1	3.3	0.358
Nondippers	13	43.3	11	36.7	
Diastolic blood pressure					
Dippers	3	10.0	0	0.0	0.255
Nondippers	15	50.0	12	40.3	
Mean arterial pressure					
Dippers	4	13.3	1	3.3	0.622
Nondippers	14	46.7	11	36.7	

	Male		Female		
Blood pressure	No.	%	No.	%	p-value
Total systolic	158.3	29.5	148.7	27.8	0.289
Active systolic	160.6	28.1	148.2	26.4	0.235
Passive systolic	154.5	33.3	144.1	30.0	0.397
Total diastolic	90.4	20.4	84.1	13.8	0.358
Active diastolic	91.3	20.2	85.2	13.5	0.372
Passive diastolic	89.2	21.4	82.4	14.2	0.345

Table 8: Circadian patterns of blood pressure by type of stroke

	Hemo	nhagic	Ischer			
Blood pressure	No.	%	No.	%	p-value	
Systolic blood pressure						
Dippers	3	10.0	3	10.0	0.300	
Nondippers	5	16.7	19	63.3		
Diastolic blood pressure						
Dippers	2	6.7	3	10.0	0.589	
Nondippers	6	20.0	19	63.3		
Mean arterial pressure						
Dippers	2	10.0	3	10.0	0.589	
Nondippers	6	20.0	19	63.3		

Table 9: Mean blood pressures by type of stroke

	Hemorrh	agic	Ischemic	Ischemic			
Blood pressure	No.	%	No.	%	p-value		
Total systolic	165.1	25.4	149.4	29.5	0.194		
Active systolic	167.8	23.4	151.2	28.2	0.148		
Passive systolic	158.6	29.9	147.0	32.7	0.390		
Total diastolic	100.8	17.1	83.2	16.3	0.015		
Active diastolic	102.0	16.7	84.1	16.0	0.012		
Passive diastolic	97.7	18.4	82.1	17.5	0.044		

patterns or mean systolic and diastolic blood pressures by sex (Table 6-7). A significant number of nondippers suffered ischemic strokes however, no significant difference was noted in the circadian patterns of patients who suffered either ischemic or hemorrhagic stroke (Table 8). The mean systolic and diastolic blood pressures were higher in hemorrhagic stroke patients than in ischemic stroke patients, although no significant difference in mean diastolic blood pressure existed when comparing types of stroke (Table 9).

The majority of patients experienced symptom onset during the day (66.7%). More patients with a nondipper pattern had onset during the day than at night. The mean systolic blood pressures were slightly higher in patients

Table 10: Circadian patterns of blood pressure by onset of stroke

	During	g day	At nig		
Blood pressure	No.	%	No.	%	p-value
Systolic blood pressure					
Dippers	4	13.3	2	6.7	1.000
Nondippers	16	53.3	8	26.7	
Diastolic blood pressure					
Dippers	5	16.7	0	0.00	0.140
Nondippers	15	50.0	10	33.3	
Mean arterial pressure					
Dippers	4	13.3	1	3.3	0.640
Nondippers	16	53.3	9	30.0	

Table 11: Mean blood pressures by onset of stroke

	During day		At night		
Blood pressure					
	No.	%	No.	%	p-value
Total systolic	152.6	29.2	155.8	29.8	0.775
Active systolic	154.6	27.8	157.8	26.7	0.767
Passive systolic	149.3	32.5	152.0	32.3	0.837
Total diastolic	88.0	17.4	87.8	20.3	0.972
Active diastolic	89.2	17.1	88.2	20.1	0.893
Passive diastolic	86.2	18.5	86.7	20.3	0.945

Table 12: Circadian patterns of blood pressure by frequency of stroke

	First attack		Recurrent		
Blood pressure	No.	%	No.	%	p-value
Systolic blood pressure					
Dippers	4	13.3	2	6.7	0.645
Nondippers	18	60.0	6	20.0	
Diastolic blood pressure					
Dippers	4	13.3	1	3.3	1.000
Nondippers	18	60.0	7	23.3	
Mean arterial pressure					
Dippers	4	13.3	1	3.3	1.000
Nondippers	18	60.0	7	23.3	

Table 13: Mean blood pressures by frequency of stroke

	First attack		Recurrent		
Blood pressure	No.	%	No.	%	p-value
Total systolic	151.7	29.2	159.0	29.4	0.553
Active systolic	153.6	27.5	161.2	29.2	0.519
Passive systolic	148.1	32.2	156.9	32.1	0.533
Total diastolic	87.2	17.9	89.8	19.6	0.734
Active diastolic	88.2	17.2	90.7	20.6	0.739
Passive diastolic	85.6	19.1	89.0	19.1	0.681

with symptoms onset at night compared with patients with onset during the day but diastolic blood pressures were not significantly different between the two periods of onset. There were no significant differences in circadian patterns or mean systolic and diastolic blood pressures relative to the onset of stroke symptoms (Table 10-11).

The majority of patients (73.3%) suffered their first stroke. More nondippers suffered their first attack than a recurrence of stroke but the mean systolic and diastolic blood pressures were higher in the recurrent stroke group. There were no significant differences in circadian patterns or mean systolic and diastolic blood pressures relative to stroke frequency (Table 12-13).

DISCUSSION

Circadian rhythm is a prognostic marker in hypertensive patients (Larochelle, 2002). A nocturnal fall in blood pressure occurs in both normotensive subjects and hypertensive patients (Larochelle, 2002; Kario *et al.*, 2000). Patients experiencing an absence of a nocturnal fall in blood pressure are known as nondippers and their pattern is more common in subjects with hypertension. Various studies show that this pattern tends to be associated with target organ damage (Caplan, 2000; Jain *et al.*, 2000; Kaplan, 1998) and damage related to ambulatory blood pressure (Mancia and Parati, 2000; Verdecchia *et al.*, 1994). Ohkubo *et al.* (2000) found that ambulatory blood pressure values have a linear relationship to stroke risk and are therefore, a strong predictor of stroke risk.

Hypertension is major risk factor for stroke (Caplan, 2000) and is also a prognostic indicator in patients who have suffered a stroke (Jain et al., 2000). Morning surges in blood pressure are associated with stroke events (Kario et al., 2003). In this study, most stroke patients (86.7%) had a history of hypertension but only 20 (66.7%) were taking antihypertensive medications. Our results are similar to the findings of Von Kanel et al. (2004), who investigated the relationship between circadian rhythm and acute stroke and found that 62% (31) of their patients had a history of hypertension. Hypertension predisposes the patient to stroke occurrence via atherosclerosis, which may trigger complications in the brain as a result of pre-existing heart disease (Jain et al., 2000). Von Kanel et al. (2004) studied the relationship between blood pressure patterns and procoagulant proinflammatory mediators in both normotensive patients and 76 patients with untreated hypertension and found that the blood pressure patterns of nondippers are associated with an increase in mediators that play a role in both endothelial dysfunction and atherosclerosis.

In this study, blood pressure measurements were divided into 6 sections; two peaks were noted between 4 and 8 a.m. and 12 and 4 p.m. (23.3%) and minimum blood pressures were noted between 12 and 4 a.m. (9.6%). Our study demonstrated that the majority of patients in this study were nondippers. Von Kanel *et al.* (2004) studied 50 acute stroke patients who were admitted to the hospital and underwent blood pressure measurements at 15 min intervals during the day (6 a.m. until 6 p.m.) and at 20 min intervals at night (6 until 6 a.m.). They found that nondippers accounted for 44 (88%) of the patients and that these patients were at a higher risk for target organ damage. Yamamoto *et al.* (1998) studied 105 patients with lacunar infarcts and found that both high nocturnal blood

pressures and declines in nocturnal blood pressure are associated with a greater number of lesions in the setting of ischemic strokes and lacunar infarcts. Kario *et al.* (2001) identified a difference in the incidence of stroke in people with hypertension that is related to the reduction of blood pressure in the evening. Patterns characterized by no changes or extreme changes in blood pressure are predictors of stroke in patients with hypertension.

Our study showed that the nondipper pattern was the most common blood pressure pattern observed in patients with acute stroke based on systolic, diastolic and mean arterial blood pressures. The number of nondippers was greater in patients aged 57 years or younger, male patients, patients with ischemic stroke, patients with symptom onset during the day and patients suffering their first strokes, compared with patients aged 57 years or older, female patients, patients with hemorrhagic stroke, patients with symptom onset at night and patients experiencing stroke recurrence, respectively. However, there were no significant differences in the circadian patterns of the two groups when age, sex, stroke type, symptom onset and symptom frequency were considered.

The mean total, active and passive systolic blood pressures were higher in the group older than 57 years of age (157.5±29.9, 159.0±29.2 and 155.6±3.1, respectively), whereas the mean total, active and passive diastolic blood pressures were higher in the younger age group (91.5±19.5, 93.0±18.3 and 88.8±21.4, respectively). However, the mean systolic and diastolic blood pressures between the two groups were not significantly different. High blood pressure is more common during middle age and in elderly people. High blood pressure damages blood vessels, causing them to become atherosclerotic. This plaque formation results in occlusion that may cause ischemic stroke and may also cause blood vessels to weaken and burst, resulting in bleeding (hemorrhagic stroke). A meta-analysis of 9 prospective studies over 10 years found that the risk of stroke increased by 46% with each 7.5 mm Hg rise in diastolic blood pressure (Sacco and Albala, 2001).

The mean total, active and passive systolic and diastolic blood pressures were respectively higher in males (systolic: 158.3±29.5, 160.6±28.1 and 154.5±33.3 and diastolic: 90.4±20.4, 91.3±20.2 and 89.2±21.4) compared with females (systolic: 148.7±27.8, 148.2±26.4 and 144.1±30.0 and diastolic: 84.1±13.8, 85.2±13.5 and 82.4±14.2). The mean systolic and diastolic blood pressures were not different between males and females and there was no significant difference in circadian blood pressures between males and females. These findings are similar to those of Lip *et al.* (1997), who studied 86 patients with acute stroke (48 male and 38 female) and

found no differences in blood pressure between male and female patients. There was also no significant difference between mean daytime and night-time systolic blood pressures, although the mean daytime diastolic blood pressures were higher than the night-time diastolic blood pressures.

The mean total, active and passive systolic and diastolic blood pressures were respectively higher in patients with hemorrhagic stroke (systolic: 165.1±25.4, 167.8±23.4 and 158.6±29.9 and diastolic: 100.8±17.1, 102.0±16.7 and 97.7±18.4) compared with patients with ischemic stroke (diastolic: 149.4±29.5, 151.2±28.2 and 147.0±32.7 and diastolic: 83.2±16.3, 84.1±16.0 and 82.1±17.5). The mean systolic and diastolic blood pressures relative to stroke type were not significantly different. Ischemic stroke was more common than hemorrhagic stroke among nondippers. However, there was no significant difference in circadian blood pressures between the ischemic and haemorrhage stroke groups. These findings are similar to those of Jain et al. (2000), who found that systolic and diastolic blood pressures were higher in patients with hemorrhagic stroke (172±24 and 105±19, respectively) compared with patients with ischemic stroke (150±36 and 89±18, respectively). Fortyfour patients (88%) were nondippers. Ajayi et al. (2013) studied 61 patients with acute stroke, 34 of whom met the inclusion criteria of presentation within 72 h of symptom onset and found that the mean daytime, night-time and 24 h blood pressures were higher in patients who suffered hemorrhagic stroke than ischemic stroke. Of the 34 patients in question, 22 were nondippers and there were significant differences in circadian blood pressures between both dippers and nondippers and between hemorrhagic and ischemic stroke patients.

Twenty patients (66.7%) presented with the onset of stroke symptoms during the day and 10 (33.3%) presented with symptom onset at night. Onset during the day occurred from 6 a.m to 10 p.m, whereas night-time onset occurred from 10 p.m. to 6 a.m. This study revealed that blood pressure peaked between 4 a.m. and 8 p.m. and between 12 and 4 p.m. These increases in blood pressure coincided with the peak incidences of stroke. These findings are similar to those of Lago et al. (1998), who studied 1,223 patients with acute stroke to investigate circadian variations in blood pressure. They found that 25.6% of patients with stroke experienced symptom onset during the day and that the highest incidence occurred in the early hours of the morning, with morning referring to the interval between 6 a.m and noon. A meta-analysis of 31 publications reporting the circadian rhythms of 11,816 patients showed that there is pattern in the onset of stroke and the period of highest risk occurs during

early morning (Elliott, 1998). Mean systolic blood pressures are slightly higher at night than during the day, whereas mean diastolic blood pressures are not different between the two time periods. The blood pressures of nondippers who experienced the onset of stroke symptoms during the day were higher than those patients who experienced symptom onset at night. Stergiou *et al.* (2002) studied 379 patients with acute stroke to investigate diurnal variations in blood pressure and found significance differences in the mean systolic and diastolic blood pressures between patients who experienced symptom onset during the day compared with those whose symptoms began at night (Stergiou *et al.*, 2002).

The mean total, active and passive systolic and diastolic blood pressures were respectively higher in patients with recurrent stroke (systolic: 159.1±29.4, 161.2±29.2 and 156.9±32.1 and diastolic: 89.8±19.6, 90.7±20.6, 89.0±19.1) compared with patients who suffered their first event (systolic: 151.7±29.2, 153.6±27.5 and 148.1±32.2 and diastolic: 87.2±17.9, 88.2±17.2 and 85.6±19.1). The proportion of nondippers was higher in the group of patients who suffered their first strokes than it was in the recurrent stroke group. However, there were no differences in the mean systolic and diastolic blood pressures or in the circadian patterns between these two groups. These findings are similar to those of study by Lago et al. (1998), who investigated 1,223 patients with acute stroke to determine its relationship to circadian rhythm and identified a difference in circadian variations of blood pressure between the groups in question.

LIMITATION

A limitation of this study is the small sample size that met the inclusion criteria and could participate in the 24 h blood pressure monitoring. The further studies are needed with more sample sizes and so the result may be generalized.

CONCLUSION

This study revealed that hypertension is a major risk factor for stroke and that the most common blood pressure pattern associated with it is characterized by the absence of a nocturnal BP decrease. This nondippers pattern is associated with target organ damage. Otherwise, circadian variations in blood pressure used as prognostic markers in hypertensive patients. Although, nondippers were more common than dippers, however we did not find significant differences in circadian patterns by age, sex, stroke type or onset and frequency of stroke symptoms. Likewise, there were no significant differences

in mean of blood pressures in relation to age, sex, stroke type or onset and frequency of stroke symptoms. Therefore, to prevent stroke and stroke recurrence, 24 h blood pressure monitoring is necessary to determine the circadian patterns of blood pressure. These patterns may then be used to identify appropriate dosages of antihypertensive medications.

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REFERENCES

- Ajayi, A.O., E.A. Ajayi, K.A. Adekeye and O.A. Busari, 2013. Pattern of circadian rhythm of blood pressure in acute stroke. Wudpecker J. Med. Sci., 2: 15-20.
- Anderson, N., V. Feigin, D. Bennett, C. Anderson, J. Broad, M. Pledger and R. Bonita, 2004. Diurnal, weekly and seasonal variations in stroke occurrence in a population-based study in Auckland, New Zealand. N. Z. Med. J., Vol. 117.
- Caplan, L.R., 2000. Caplan's Stroke: A Clinical Approach. 3rd Edn. butterworth Heinemann, Boston, USA., pp. 1-7.
- Elliott, W.J., 1998. Circadian variation in the timing of stroke onset: A meta-analysis. Stroke, 29: 992-996.
- Grassi, G., B.M. Cattaneo, G. Seravalle, A. Lanfranchi and G. Mancia, 1998. Baroreflex control of sympathetic nerve activity in essential and secondary hypertension. Hypertension, 31: 68-72.
- Jain, S., K.K. Namboodri, S. Kumari and S. Prabhakar, 2000. Loss of circadian rhythm of blood pressure following acute stroke. BMC Neurol., Vol. 4. 10.1186/1471-2377-4-1
- Kalim, H., 2009. 24 hour-blood pressure and target organ damage. Proceedings of the Symposium on Recent Development in Prevention of Stroke, (RDPS'09), Padang, Indonesia.
- Kaplan, N.M., 1998. Lieberman E. Clinical Hypertension. 5th Edn., William and Wilkins, USA.
- Kario, K., T. Matsuo, H. Kobayashi, M. Imiya, M. Matsuo and K. Shimada, 1996. Nocturnal fall of blood pressure and silent cerebrovascular damage in elderly hypertensive patients: Advanced silent cerebrovascular damage in extreme dippers. Hypertension, 27: 130-135.

- Kario, K., J.E. Schwartz and T.G. Pickering, 2000. Changes of nocturnal blood pressure dipping status in hypertensives by nighttime dosing of alpha-adrenergic blocker, doxazosin: Results from the HALT study. Hypertension, 35: 787-794.
- Kario, K., T.G. Pickering, T. Matsuo, S. Hoshide, J.E. Schwartz and K. Shimada, 2001. Stroke prognosis and abnormal nocturnal blood pressure falls in older hypertensives. Hypertension, 38: 852-857.
- Kario, K., T.G. Pickering, Y. Umeda, S. Hoshide and Y. Hoshide *et al.*, 2003. Morning surge in blood pressure as a predictor of silent and clinical cerebrovascular disease in elderly hypertensives: A prospective study. Circulation, 107: 1401-1406.
- Lago, A., D. Geffner, J. Tembl, L. Landete, C. Valero and M. Baquero, 1998. Circadian variation in acute ischemic stroke: A hospital-based study. Stroke, 29: 1873-1875.
- Larochelle, P., 2002. Circadian variation in blood pressure: Dipper or nondipper. J. Clin. Hypertension, 4: 3-8
- Lip, G.Y., J. Zarifis, I.S. Farooqi, A. Page, G. Sagar and D.G. Beevers, 1997. Ambulatory blood pressure monitoring in acute stroke: The West Birmingham stroke project. Stroke, 28: 31-35.
- Mancia, G. and G. Parati, 2000. Ambulatory blood pressure monitoring and organ damage. Hypertension, 36: 894-900.
- Nakamura, K., J. Oita and T. Yamaguchi, 1995. Nocturnal blood pressure dip in stroke survivors: A pilot study. Stroke, 26: 1373-1378.
- Ohkubo, T., A. Hozawa, K. Nagaie, M. Kikuya and I. Tsujia *et al.*, 2000. Prediction of stroke by ambulatory blood pressure monitoring versus screening blood pressure measurements in a general population: The Ohasama study. J. Hypertens., 18: 847-854.
- Sacco, R.L. and B. Albala, 2001. Stroke Risk Factors: Identification and Modification. In: Stroke Therapy, Fischer, M. (Ed.). 2nd Edn. butterworth-Heinemann, Boston, USA., pp. 1-24.
- Stergiou, G.S., K.N. Vemmos, K.M. Pliarchopoulou, A.G. Synetos, L.G. Roussias and T.D. Mountokalakis, 2002. Parallel morning and evening surge in stroke onset, blood pressure and physical activity. Stroke, 33: 1480-1486.
- Verdecchia, P., C. Porcellati, G. Schillaci, C. Borgioni and A. Ciucci et al., 1994. Ambulatory blood pressure. An independent predictor of prognosis in essential hypertension. Hypertension, 24: 793-801.

- Von Kanel, R., S. SJain, P.J. Mills, R.A. Nelesen and K.A. Adler *et al.*, 2004. Relation of nocturnal blood pressure dipping to cellular adhesion, inflammation and hemostasis. J. Hypertens., 22: 2087-2093.
- WHO, 1978. Cerebrovascular disorder: A clinical and research classification. WHO Offset Publication No. 43, World Health Organization (WHO), Geneva, Switzerland, pp. 1-82.
- Watanabe, N., Y. Imai, K. Nagai, I. Tsuji and H. Satoh *et al.*, 1996. Nocturnal blood pressure and silent cerebrovascular lesions in elderly Japanese. Stroke, 27: 1319-1327.
- White, W.B., 2007. Importance of blood pressure control over a 24 h period. J. Manage. Care Pharm., 13: 34-39.
- Yamamoto, Y., I. Akiguchi, K. Oiwa, M. Hayashi and J. Kimura, 1998. Adverse effect of nighttime blood pressure on the outcome of lacunar infarct patients. Stroke, 29: 570-576.
- Yung, S.P., W.S. Jung, S.K. Moon, K.H. Cho and Y.S. Kim, 2007. Circadian variation of acute stroke: Hospital based study. Korean J. Orient. Med., 28: 8-12.